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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/057,646 | 01/25/2002 | Harry R. Davis | CV01379K | 3480 |

24265 7590 12/20/2005

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PATENT DEPARTMENT (K-6-1, 1990)
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| EXAMINER | |
|---|---|
| WANG, SHENGJUN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1617 | |

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/057,646 | DAVIS ET AL. | |
| | Examiner | Art Unit | |
| | Shengjun Wang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,7-30 and 32* is/are pending in the application.

4a) Of the above claim(s) *11-27,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10,28 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. In view of the appeal brief filed on September 20, 2005, PROSECUTION IS HEREBY REOPENED. A new ground of rejections set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Sreeni Padmanabhan.

### *Restriction Requirements*

Applicants have elected with traverse of invention directed to a composition, and the claims have been examined insofar as they read on the elected invention and species. See, office action mailed November 12, 2003. It is noted that claim 28 and 29, which are directed to a method, are inadvertently listed as rejected composition claims. Claims 28 and 29 are withdrawn from further consideration as they are directed to non-elected invention.

***Claim Rejections 35 U.S.C. 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of vascular condition, diabetes or obesity, does not reasonably provide enablement for prevention of such disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The application shows the claimed composition is useful in treating, or suppressing the symptoms of vascular conditions, diabetes or obesity.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claims recite prevention of vascular condition, diabetes, or obesity. The application provides no guidance, direction or working examples as to the prevention of such disorders. The state of the prior art indicates that the disorders herein recited may arise from a variety of etiologies. While there are methods for controlling or suppressing the progress of the conditions, no method for curing or preventing such disorders is known in the art. Persons skilled in the art have been challenged to find an effective way for controlling the epidemic development of the disorders recited herein with little success. See, e.g., Laakso et al. Popkin et al. and the Merck Manual. Applicants is claiming a subject matter that skilled artisan have been worked for years but never fully achieved. Applicants fail to provide information allowing skilled artisan to ascertain such prevention without undue experimentation. In the instant case, no prevention example is set forth, thereby failing to provide sufficient working examples. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. Lowering cholesterol and/or plasma lipids may control or suppress the progress of diabetes, vascular condition, or obesity. However, the application fails to provide any guidance, direction, working example, or rationale that the claimed composition would be effective in preventing diabetes, vascular condition, or obesity.

***Claim Rejections 35 U.S.C. 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, 7-10, 28, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,846,966, IDS), in view of Kim (US 5,698,527, IDS) and Keller et al (WO 00/38725, IDS).

3. Rosenblum teaches the instant cholesterol absorption inhibitors and its application for lowering serum cholesterol. Rosenblun further teaches that the cholesterol absorption inhibitors may be employ in combination with other cholesterol lowering agents, such as simvastatin. See, particularly, the abstract, and the claims. Rosenblum et al. teach that daily dosage of the compounds is about 5mg to 1000 mg, given in a single dose or 2-4 divided doses. When used in combination with other drug the dose is about 1mg to 1000 mg a dose given 1 or 2 times a day. The exact dose would depend on various conditions. See, particularly, col. 21, lines 17-63.

4. Rosenblun et al. do not teach expressly a combination of the cholesterol absorption inhibitor and nicotinic acid.

5. However, Kim teaches that nicotinic acid (niacin) is a well-known cholesterol lowering agents, and is particularly useful in combination with cholesterol absorption inhibitors. See, particularly, the abstract, and column 32, lines 9-25. Keller et al. teaches various combinations of cholesterol lowering agents, including ezetimibe and nicotinic acid, for treating hypercholesterolemia-associated disorders. See, particularly, the abstract, and pages 11-14.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a composition comprising ezatimibe and nicotinic acid, and optionally simvastatin.

A person of ordinary skill in the art would have been motivated to make a composition comprising ezatimibe and nicotinic acid, and optionally simvastatin because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known cholesterol lowering sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. Further, the prior art have suggested the usefulness of combination of different cholesterol lowering agents, particularly, cholesterol absorption inhibitor and nicotinic acid. As to the specific amount of ezatimibe, note the amount (10 mg) is within the range disclosed by Rosenblum et al. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Further, Optimization Within Prior Art Conditions or Through Routine Experimentation Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

***Response to the Arguments***

6. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The references herein relied upon establish a strong prima facie case of obviousness as to applicants' invention. The claimed subject matter is of such a nature that the differences between said subject matter, and the teachings of the prior art of record, would have rendered applicants' subject matter, as a whole, obvious to those skilled in the art at the time of applicants' invention. The references clearly establish that the claim designated components were old, of known character and that one skilled in the art would have been motivated to employ said components in the manner herein claimed to obtain the claimed, expected results. The claims are therefore properly rejected under 35 USC 103. Applicants' arguments fail to reach the instant rejections core issue; that concomitantly employing compounds, old and well known for the same use is obvious to the skilled artisan. To overcome this rejection Applicants must illustrate the presence of unexpected benefits in the resulting mixture. Any combination not shown to possesses such unexpected benefits must remain properly rejected as obvious. In illustrating unexpected therapeutic benefits the Applicant must test all active components individually to ensure a greater than additive therapeutic benefit.

The arguments of commercial success are deemed unpersuasive. Note the success commercial product is ZETIA™ (ezetimibe), note the claimed combination.

For reasons discussed above, all the claims have been properly rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shengjun Wang
Primary Examiner
Art Unit 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER